Synopsis

Name of Research Scholar: Prabhnain Kaur **Name of Supervisor:** Prof. Ravichandiran V

Registration No.: 02/Ph.D./DPSRU/2020

Title of Thesis: "Development and Investigation of Herbal Formulation Targeting NF-kB for the Treatment of Diabetic Complications Using Experimental Animal Model"

Abstract of work done

Introduction: The proposed work focused on evaluating the protective effect of a herbal formulation/combination consisting of Moringa oleifera extract (MO) (100 mg/kg), Withania somnifera extract (200 mg/kg), Momordica charantia (200 mg/kg) and Terminalia arjuna extract (500 mg/kg) in the management of diabetic complications via modulation of NF-κB, ICAM-1/VCAM-1 signaling pathway.

Objective:

1. To perform docking studies on the major constituents of the selected herbal extracts.
2. To study the protective effects of herbal combination on streptozotocin-induced diabetic retinopathy.
3. To study the protective properties of herbal combination in streptozotocin-induced diabetic cardiomyopathy.
4. To study the therapeutic efficacy of herbal combination in streptozotocin-induced diabetic nephropathy.
5. To develop an appropriate dosage form of the herbal combination for clinical application.

Milestones of the thesis with DSRC AND URAC dates

DSRC	Date	URAC	Date
DSRC 1st	August 26, 2021	1st	2022
DSRC 2nd	November 02, 2022	2nd	April 11, 2023

DSRC 3rd	November 21, 2023	3rd	June 10, 2024
DSRC 4th	October 08, 2024	4th	March 24, 2025

Methodology: Type I diabetes was induced in Wistar rats through a single intraperitoneal injection of Streptozotocin at 45 mg/kg. Rats with blood glucose levels exceeding 300 mg/dl were considered diabetic. These rats were divided into two groups and subjected to a 24-week treatment regimen using a polyherbal combination of MO (100 mg/kg), WS (200 mg/kg), MC (200 mg/kg), and TA (500 mg/kg). An age-matched control group was also included. Regular assessments were performed, measuring blood glucose levels, body weight. The functional parameters assessed for diabetic retinopathy included fundus photos, fundus angiography, and flat mount retina using FITC dextran. Additionally, biochemical markers such as VEGF, TAC, and TNF-α were analyzed. Molecular techniques, including H&E staining, IHC for NF-κB, VCAM-1, and ICAM-1, as well as PCR and WB for ICAM-1 and NF-κB, were also employed in the evaluation process. The study assessed many cardinal measures, including electrocardiography (ECG), echocardiography (ECHO), CK-MB, hs CRP, transforming growth factor-beta (TGF-β), serum cholesterol, and triglyceride levels, in order to investigate diabetic cardiomyopathy. Additionally, molecular parameters such as H&E, IHC for ICAM-1 and VCAM-1, TGF-β, NF-kB, and mRNA expression using PCR were also evaluated. For diabetic nephropathy, many key parameters including serum creatinine, urea, TGF-β, and urine analysis were carried out. Additionally, molecular parameters such as H&E, immunohistochemistry for TGF-β and ICAM-1, as well as PCR analysis were done and subsequently assessed.

Results: The findings of this study elucidate the significant protective effects of a polyherbal formulation comprising *Moringa oleifera* (MO), *Withania somnifera* (WS), *Terminalia arjuna* (TA), and *Momordica charantia* (MC) against diabetic complications, specifically retinopathy, cardiomyopathy, and nephropathy, in a streptozotocin-induced diabetic rat model. Molecular docking studies revealed that quercetin, myricetin, charantin, Withaferin A, and Arjunone exhibited strong binding affinities for the pro-inflammatory and pro-angiogenic biomarkers ICAM-1, VCAM-1, VEGF, and NF-κB, surpassing the binding efficacy of standard compounds. This suggests their potential as modulators of critical pathways involved in secondary diabetic

complications.

In vivo assessments demonstrated that the polyherbal formulation significantly decreased blood glucose levels and enhanced body weight in treated subjects, indicative of improved metabolic control. In the context of diabetic retinopathy, fundus photography and angiographic analyses revealed a notable reduction in retinal damage, paralleled by decreased levels of angiogenic and inflammatory markers such as VEGF, TAC, and TNF-α, which suggests a suppression of angiogenesis and inflammation. Immunohistochemical (IHC) and polymerase chain reaction (PCR) analyses further confirmed the downregulation of NF-κB, ICAM-1, and VCAM-1, indicating that the inhibition of the NF-κB signaling pathway is a central mechanism underlying these protective effects.

For diabetic cardiomyopathy, the polyherbal combination resulted in improvements in electrocardiographic (ECG) and echocardiographic (ECHO) parameters, as well as reductions in cardiac injury markers such as CK-MB, hs-CRP, and TGF-β, alongside decreases in inflammatory and fibrotic markers. Histopathological evaluations corroborated these findings, revealing a significant reduction in cardiac tissue damage. In diabetic nephropathy, treatment with the formulation led to decreased serum creatinine, urea, and albumin excretion levels, reflecting renal protective effects. Molecular analyses indicated a reduction in oxidative stress markers and TGF-β expression, alongside improvements in renal tissue morphology along with the significant reduction in ICAM-1, VCAM-1 level as revealed by IHC and PCR studies.

Moreover, the polyherbal combination exhibited robust stability and quality in both powder and tablet forms, fulfilling established pharmaceutical standards, thereby enhancing its potential for clinical application. Collectively, these results underscore the therapeutic efficacy of the polyherbal formulation, highlighting its anti-inflammatory, antioxidant, and anti-angiogenic properties in the management of diabetic complications. These findings warrant further investigation and clinical trials to substantiate the formulation's role in comprehensive diabetic care.

Conclusions: In conclusion, the polyherbal combination comprising Moringa oleifera, Withania somnifera, Terminalia arjuna, and Momordica charantia demonstrates significant protective effects against diabetic complications, including retinopathy, cardiomyopathy, and nephropathy, through modulation of critical biomarkers such as NF-κB, ICAM-1, and VCAM-1. These findings support its potential as a therapeutic intervention, warranting further

investigation on to establish its efficacy in diabetic management.

Scientific Relevance And Impact Of The Results: The study's findings significantly enhances the scientific data for the therapeutic potential of polyherbal formulations comprising *Moringa oleifera*, *Withania somnifera*, *Terminalia arjuna*, and *Momordica charantia* in managing diabetic complications. This research not only underscores the importance of traditional medicinal plants in contemporary diabetes treatment but also provides a scientific foundation for further exploration of these compounds as potential adjunct therapies. Future work should focus on profiling individual medicinal herb for identification, quantification and optimizing the individual content ratio for combination therapy with the targeted pathway for their potential application in future translational research.

Recommendations of URAC after 4th DSRC	**Compliance**
4th DSRC report of Ms. Prabhnain Kaur approved for thesis submission	The presentation of the report is in compliance with the designed format.

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Title	Ph D thesis
Paper/Submission ID	3505560
Submitted by	library.dipsar@yahoo.co.in
Submission Date	2025-04-15 16:55:42
Total Pages, Total Words	109, 26237
Document type	Thesis

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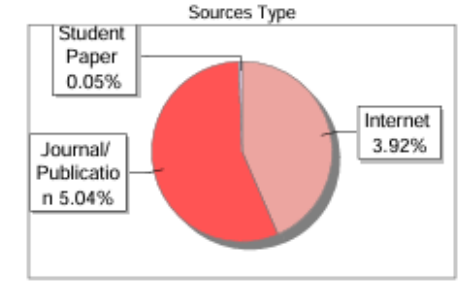

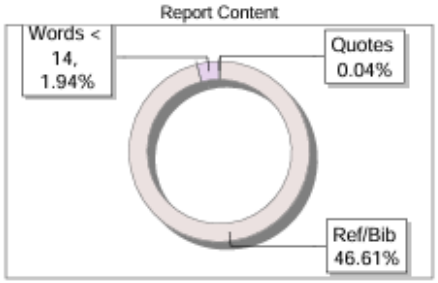

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Publication:

1. **Kaur P,** Sharma K, Goyal RK. Moringa oleifera extract ameliorates diabetic retinopathy via NF-κB and VCAM-1 pathway in streptozotocin induced diabetic rats. South African Journal of Botany. 2023 Nov 1;162:519-30.
2. **Kaur P,** Vishwakarma VK, Singh A, Goyal RK. Herbal Insights: Exploring the Therapeutic Potential of Indian Dietary Herbs in Diabetic Cardiomyopathy Management. Current Diabetes Reviews. 2024 Aug 9.
3. **Prabhnain Kaur,** Ritu, Kalicharan sharma, Ramesh K Goyal. Modulating Effect of Phenolic Compounds on The Insulin Secretion in RIN 5F Cells and Streptozotocin Induced Diabetes Rats. Afr. J. Bio. Sc. 6(5) (2024).
4. Ritu**,** Verma, R., Kaushik, S., **Kaur, P.,** Mathur, P., Velpandian, T. and Goyal, R.K., 2025. Hesperetin supplemented soybean and ginger hydroalcoholic extracts alleviate diabetic cardiomyopathy in streptozotocin induced diabetic rats by modulating NF-κB/MMP-9/TIMPs pathway. South African 3 Journal of Botany, 179, pp.11-21**.(IF -2.7)**
5. Ritu, **Prabhnain kaur,** Kanika goyal, Ayushi kumari, Ramesh K Goyal and Kalicharan Sharma. Uncovering the Impact of MMP-9 and TIMPs in Diabetic Nephropathy: A Review of Bioflavonoids in Disease Management in Current nutraceuticals.
6. **Kaur P,** Dahiya R, Nandave M, Sharma K, Goyal RK. Unveiling the crucial role of intercellular adhesion molecule-1 in secondary diabetic complications. Cell Biochem Funct. 2024;42:e4037. doi:10.1002/cbf.4037. **(IF-3**)
7. **Kaur, P.,** Sharma, K., Goyal, R. K., Basist, P., Khan, R., Alhalmi, A., & Dahiya, R. (2024). Unveiling VCAM-1's Multifaceted Role in Secondary Diabetic Complications. Journal of Food Quality, 2025(1), 9206712.(IF-3)
8. **Kaur P,** Ritu, Sharma K, Goyal RK. Mitigating Diabetic Cardiomyopathy: The Therapeutic Potential of a Poly Herbal Combination in Modulating ICAM-1, VCAM-1, and NF-κB Expression in Rat Model. Cardiovasc Hematol Disord Drug Targets. 2025 Jul 9.

Book chapter

1. **Prabhnain Kaur**, Ritu Dahiya, Ginpreet Kaur, Harpal S. Buttar, Douglas W. Wilson, Istvan G. Telessy ; Pathogenesis of Atherosclerosis and Coronary Heart Disease:

Epidemiology, Diagnostic Biomarkers and Prevention by Nutraceuticals, Functional Foods, and Plant-Derived Therapies, Botanicals and Natural Bioactives: Prevention and Treatment of Diseases Bentham Briefs in Biomedicine and Pharmacotherapy (2024) 2: 146. https://doi.org/10.2174/9789815238273124020010

2. **Kaur, P**., Dahiya, R., Buttar, H.S., Wilson, D.W., De Meester, F., Telessy, I.G. (2024). Antiatherogenic Effects of Vitamins, Mediterranean Diet and DASH Diet: An Overview for the Prevention of Cardiovascular Diseases. In: Shah, A.K., Tappia, P.S., Dhalla, N.S. (eds) Hydrophilic Vitamins in Health and Disease. Advances in Biochemistry in Health and Disease, vol 29. Springer, Cham. Chapter 3, 4 Pages 45-66 https://doi.org/10.1007/978-3-031-55474-2_3
3. Gholami M, Salmani RH, Madadlou SK, Khoshraftar P, Buttar HS, Abbasi-Maleki S, **Kaur P.** Antidepressant effects of medicinal plants and their pharmacologically active ingredients: A systematic review focused on the serotonergic system. Molecular Medicine and Biomedical Research in the Era of Precision Medicine. 2025 Jan 1:261-78.
4. **Kaur P,** Buttar HS, Wilson DW, Télessy IG, Garg VK. Multifaceted benefits of anthocyanins and their derivatives in health and disease: A systematic review. Molecular Medicine and Biomedical Research in the Era of Precision Medicine. 2025 Jan 1:1045-97.

Conference/workshop/seminars:

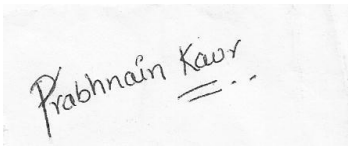
Oral presentations

1. Awarded **Best Oral Presentation** for the paper entitled "Moringa oleifera extract ameliorates Diabetic Retinopathy Via NF-κB and VCAM-1 Pathway in STZ induced Diabetic Rats" in the 2nd International Conference on Natural Products and Human Health-2022, held at Deshbandhu College, University of Delhi.
2. Presented oral presentation at Annual CME DC-ISAR- 2023 on "Efficacy and safety of *Terminalia arjuna* in coronary artery disease" held on 3rd Nov 2023, at Lady Hardinge Medical College, New Delhi.

CONFERENCES ATTENDED

1. Attended International Symposium on "Safety Assesment Under Materiovigilance and Pharmacovigilance Programs" held at Delhi Pharmaceutical Sciences and Research University, Delhi.

2. Attended 2nd International Conference on Natural Products and Human Health-2022, held at Deshbandhu College, University of Delhi, India
3. Awarded Best Oral Presentation for the paper entitled “Moringa oleifera extract ameliorates Diabetic Retinopathy via NF-κB and VCAM-1 Pathway in STZ induced Diabetic Rats” in the 2nd International Conference on Natural Products and Human Health-2022, held at Deshbandhu College, University of Delhi.
4. Attended Annual conference- DPSCON 2023 on “Advances & Current Trends in Pharmacology” held at DPSRU, New Delhi.
5. Presented poster at Indian eye research group (ARVO) -2023 on “Poly Herbal Combination (PHC) Ameliorates Diabetic Retinopathy via NF-κB And VCAM-1 Pathway In Streptozotocin Induced Diabetic Rats” held on 28-30 July 2023 held at Madurai, India.



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Annexure

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Natural Products and Human Health - 2022
November 4th – 6th, 2022

Certificate of Excellence

for Best Oral Presentation

Awarded to Prabhnain Kaur

For the paper entitled "*Moringa oleifera* Extract ameliorates Diabetic Retinopathy via NF-kB and VCAM-1 Pathway In Streptozotocin Induced Diabetic Rats"

in the conference **ICNPHH – 2022** held at Deshbandhu College, University of Delhi, New Delhi, India.

Dr. Sunil Kayesth
Coordinator, ICNPHH 2022

Prof. Kamal Kumar Gupta
Vice Principal, Deshbandhu College

Prof. Rajiv Aggarwal
Principal, Deshbandhu College

ARVO-INDIA

Indian Eye Research Group

July 29-30, 2023

Certificate of Participation

This is to certify that

Prabhnain Kaur

participated and presented a paper/poster in the meeting held at Aravind Medical Research Foundation, Madurai.

Prof. K. Dharmalingam
President, ARVO-India

Dr. A. Vanniarajan
on behalf of Organisers

ANNUAL CME DC-ISAR 2023

"Holistic Approach to the Management of Coronary Artery Disease"

CERTIFICATE

OF PARTICIPATION

This is to certify that Ms. Prabhnain Kaur

had participated in ORAL / ~~POSTER~~ PRESENTATION in the

Annual CME DC-ISAR 2023

held at Lady Hardinge Medical College, New Delhi on 3rd November 2023

R. Singh

Dr. Ritu Singh
President, DC-ISAR

Dr. Harshvardhan Singh
Secretary, DC-ISAR

Organised by
Department of Biochemistry, Lady Hardinge Medical College, New Delhi
under the aegis of
The Delhi Chapter of Indian Society for Atherosclerosis Research

DELHI PHARMACOLOGICAL SOCIETY

2nd Annual Conference

DPSCON 2023

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This is to certify that Prof./Dr./Mr./Ms. Prabhnain Kaur *has participated as Chairperson/Invited Speaker/Presenter in scientific session/Delegate in the conference held on 1st March, 2023 at DPSRU, Pushp Vihar, New Delhi.*

Prof. RK Goyal
Chairman, DPS

Prof. T Velpandian
General Secretary, DPS

Prof. K Gulati
Treasurer, DPS

School of Medical & Allied Sciences

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CERTIFICATE OF PARTICIPATION

This is to certify that

Prof./Dr./Mr./Ms……**Prabhnain Kaur**…… ……

From ……**Delhi Pharmaceutical Sciences and Research University**……

has presented a oral presentation On ……**Mitigating Diabetic Cardiomyopathy: The Therapeutic Potential of a Poly Herbal Combination in Modulating ICAM-1, VCAM-1, and NF-κB Expression in Rat Model**

5th International Conference on "Precision Healthcare: A Holistic Step Ahead"

organized by School of Medical & Allied Sciences (SoMAS), at GD Goenka University, GD Goenka Education City, Sohna Road, Gurugram, held between 14th to 16th March 2024.

Dr. Anand Kumar Singh
Associate Professor and Head, Department of Physiotherapy
School of Medical and Allied Sciences

Dr. Anitha Arvind
Associate Professor and Head, Department of Optometry
School of Medical and Allied Sciences

Prof. (Dr.) Saahil Arora
Dean, School of Medical & Allied Sciences

South African Journal of Botany 162 (2023) 519–530

Contents lists available at ScienceDirect

South African Journal of Botany

journal homepage: www.elsevier.com/locate/sajb

Moringa oleifera extract ameliorates diabetic retinopathy via NF-κB and VCAM-1 pathway in streptozotocin induced diabetic rats

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ARTICLE INFO

Article History:
Received 7 August 2023
Revised 30 August 2023
Accepted 21 September 2023
Available online xxx

Edited by: Dr S.C. Pendota

Keywords:
Moringa oleifera
Diabetic retinopathy
Antiinflammatory
NF-κB
VCAM-1

ABSTRACT

Diabetes is a major cause of mortality and morbidity worldwide, leading to various complications, including diabetic retinopathy (DR), which can result in vision impairment and blindness. DR involves the disruption of the blood retinal barrier (BRB) and the development of neovascularization due to high blood sugar levels. Inflammatory cytokines and cell adhesion molecules play a role in this process, with NF-κB and its down regulators, such as ICAM-1 and VCAM-1, being key players. *Moringa oleifera* (MO), a plant with medicinal properties, is being investigated for its prospective effect in preventing and treating DR. This study explores the effects of *Moringa oleifera* extract on streptozotocin (STZ) induced diabetic rats with DR. Molecular docking studies indicate that components of *Moringa oleifera* extract, namely Quercetin and Myrecetin, strongly bind to key targets involved in DR.

To induce DR, rats were given STZ, and after 8 weeks, various factors were evaluated. The results show that *MO* extract significantly reduces blood glucose levels compared to the diabetes group. Additionally, the extract decreases the expression of VEGF, an angiogenic mediator, and reduces the levels of TNF-α and Total Antioxidant Capacity (TAC), markers of inflammation, in the retinas of diabetic rats. Histopathological analyses reveal improvements in the retinal blood vessels of *MO*-treated animals compared to the diabetes group. The extract also reduces the overexpression of NF-κB and VCAM-1 in the retina. These findings suggest that *MO* may be useful in managing diabetic retinopathy by inhibiting angiogenic mediators and regulating NF-κB and VCAM-1.

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1. Introduction

Diabetes is the most widespread chronic metabolic diseases, afflicting more than 8.5 % of the world's young. According to recent global statistics, 463 million have diabetes and 374 million people have glucose intolerance i.e. prediabetic condition. It was expected that these number will increase exponentially to 51 % by 2045. It is important to mention here that from 2000 to 2015, the prevalence of diabetes in India increased from 5.8 % to 8.7 % (Atlas, 2019; Pradeepa and Mohan, 2017). Persistent hyperglycaemia has catastrophic consequences on the vasculature, resulting in various micro- and macrovascular problems, such as neuropathy, nephropathy, retinopathy, and cardiomyopathy (He and King, 2004). According to the 2018, World Health Organization (WHO) Fact Sheet, diabetes was the seventh largest cause of mortality in 2016 and a primary cause of heart attack, blindness, renal failure and stroke. In diabetic individuals, hyperglycaemia-induced oxidative stress is a major contributor to cardiovascular dysfunction (CVD), retinopathy, and nephropathy. Constant hyperglycaemia elevates the expression of adhesion molecules, such as intracellular cell adhesion molecule (ICAM-1) and vascular cell adhesion molecule (VCAM-1), endothelial- leucocyte adhesion molecule (E selectins) and growth factors, such as Transforming growth factor-beta (TGF-β) and vascular endothelial growth factor (VEGF), which are implicated in a variety of diabetes problems. One of the primary causes of visual impairment in the worldwide working class is Diabetic Retinopathy (DR). Diabetic retinopathy can affect both type 1 and type 2 diabetics. The longer a person has diabetes and the less well his or her blood sugar is regulated, the greater the likelihood that he or she may develop this eye issue. According to a data sheet provided by the WHO in October 2011, 90 % of the visually impaired population resided in poor nations. Chronic hyperglycaemia produces oxidative stress, which in turn stimulates the expression of these cell adhesion molecules (CAM), as well as nuclear factor kappa B (NF-κB) and growth factors such as VEGF and TGF-β. Also, vascular dysfunction is associated with the over expression of tumour necrosis factor (TNF-α), interleukins, TGF-β and other pro-inflammatory proteins and pro-apoptotic genes (Suryavanshi and Kulkarni, 2017).

The transcription of numerous molecules linked to inflammation and pro inflammatory responses, Such as CAM, cytokines and various

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https://doi.org/10.1016/j.sajb.2023.09.040
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Review › Cell Biochem Funct. 2024 Jun;42(4):e4037. doi: 10.1002/cbf.4037.

Unveiling the crucial role of intercellular adhesion molecule-1 in secondary diabetic complications

Prabhnain Kaur [1], Ritu Dahiya [1], Mukesh Nandave [1], Kalicharan Sharma [2], Ramesh K Goyal [1]

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PMID: 38736204 DOI: 10.1002/cbf.4037

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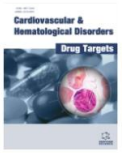

Mitigating Diabetic Cardiomyopathy: The Therapeutic Potential of a Poly Herbal Combination in Modulating ICAM-1, VCAM-1, and NF-κB Expression in Rat Model

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Authors: Prabhnain Kaur[1], Ritu[1,2], Kalicharan Sharma[3] and Ramesh Kumar Goyal[1]

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Source: Cardiovascular & Haematological Disorders - Drug Targets

Available online: 09 July 2025

DOI: https://doi.org/10.2174/011871529X374139250629193251

Received: 13 Dec 2024 **Accepted:** 19 Mar 2025 **Available online:** 09 Jul 2025

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Background

Diabetic Cardiomyopathy (DCM) remains a significant health concern, necessitating innovative therapeutic approaches. This study explores the potential of a polyherbal combination (PHC) in mitigating DCM and delves into the underlying molecular

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Prabhnain Kaur, Ritu, Kalicharan Sharma, Ramesh K. Goyal, Parakh Basist, Rahmuddin Khan, Abdulsalam Alhalmi

First published: 19 June 2025 | https://doi.org/10.1155/jfq/9206712

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https://doi.org/10.33472/AFJBS.6.5.2024.4120-4129

African Journal of Biological Sciences

Modulating Effect of Phenolic Compounds on The Insulin Secretion in RIN 5F Cells and Streptozotocin Induced Diabetes Rats

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South African Journal of Botany
Volume 179, April 2025, Pages 11-21

Hesperetin-supplemented soybean and ginger hydroalcoholic extracts alleviate diabetic cardiomyopathy in streptozotocin induced diabetic rats by modulating NF-κB/MMP-9/TIMPs pathway

Ritu [a b], Ravinder Verma [c], Sudhir Kaushik [d], Prabhnain Kaur [a], Pooja Mathur [b], T. Velpandian [e], Ramesh K Goyal [a]

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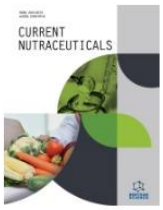
Highlights

- To explore the effect of Hesperetin, soy extract, and ginger extract on DC in rats induced by streptozotocin (STZ)
- Parameters like biochemical markers, ECG, echocardiography (ECHO), molecular pathways (NF-κB, MMP-9, TIMP-1), and histopathology were analyzed.
- Hesperetin, soy extract, and ginger extract combination significantly lowered fasting blood glucose, HOMA-IR, reduced fibrosis, improved myocardial structure and serum insulin levels.
- NF-κB, MMP-9 (promoting inflammation and tissue remodeling), and TGF-β were significantly downregulated, indicating protection against diabetic cardiac damage.



ISSN: 2665-9786
E-ISSN: 2665-9794

Uncovering the Impact of MMP-9 and TIMPs in Diabetic Nephropathy: A Review on Bioflavonoids in Disease Management

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Authors: Ritu Dahiya[1,2], Prabhnain Kaur[1], Kanika Goyal[2], Ramesh K. Goyal[1], Ayushi Singh[2] and Kalicharan Sharma[3]

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Source: Current Nutraceuticals, Volume 6, Issue 1, Jan 2025, E26659786333625
DOI: https://doi.org/10.2174/0126659786333625250114080734
Received: 27 May 2024 **Accepted:** 02 Dec 2024 **Available online:** 03 Feb 2025

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